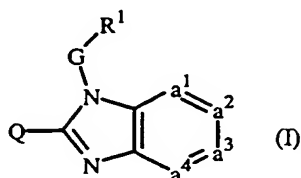


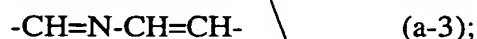
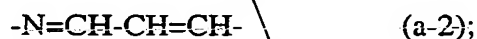
Claims

1. A compound of formula



a prodrug, *N*-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof wherein

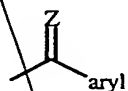
-a¹=a²-a³=a⁴- represents a bivalent radical of formula



wherein each hydrogen atom in the radicals (a-1), (a-2), (a-3), (a-4) and (a-5) may optionally be replaced by halo, C₁₋₆alkyl, nitro, amino, hydroxy,

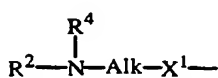
C₁₋₆alkyloxy, polyhaloC₁₋₆alkyl, carboxyl, aminoC₁₋₆alkyl, mono- or

di(C₁₋₄alkyl)aminoC₁₋₆alkyl, C₁₋₆alkyloxycarbonyl, hydroxyC₁₋₆alkyl, or a radical of formula

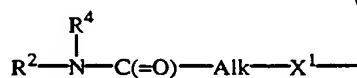


wherein =Z is =O, =CH-C(=O)-NR^{5a}R^{5b}, =CH₂, =CH-C₁₋₆alkyl, =N-OH or =N-O-C₁₋₆alkyl;

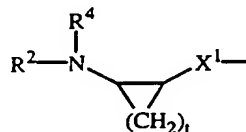
Q is a radical of formula



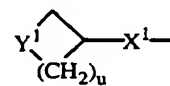
(b-1)



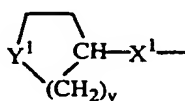
(b-2)



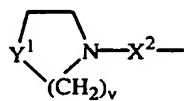
(b-3)



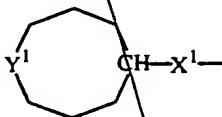
(b-4)



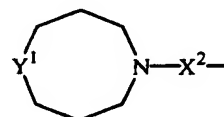
(b-5)



(b-6)



(b-7)



(b-8)

wherein Alk is C₁₋₆alkanediyl;

Y¹ is a bivalent radical of formula -NR²- or -CH(NR²R⁴)-;

X¹ is NR⁴, S, S(=O), S(=O)₂, O, CH₂, C(=O), C(=CH₂), CH(OH), CH(CH₃), CH(OCH₃), CH(SCH₃), CH(NR^{5a}R^{5b}), CH₂-NR⁴ or NR⁴-CH₂;

X^2 is a direct bond, CH_2 , $C(=O)$, NR^4 , $C_{1-4}alkyl-NR^4$, $NR^4-C_{1-4}alkyl$;

t is 2, 3, 4 or 5;

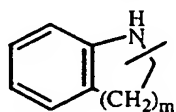
u is 1, 2, 3, 4 or 5;

v is 2 or 3; and

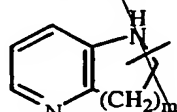
- 5 whereby each hydrogen atom in Alk and the carbocycles and the heterocycles defined in radicals (b-3), (b-4), (b-5), (b-6), (b-7) and (b-8) may optionally be replaced by R^3 ; with the proviso that when R^3 is hydroxy or $C_{1-6}alkyloxy$, then R^3 can not replace a hydrogen atom in the α position relative to a nitrogen atom;

- 10 G is a direct bond or $C_{1-10}alkanediyl$ optionally substituted with one, two or three substituents selected from hydroxy, $C_{1-6}alkyloxy$, aryl $C_{1-6}alkyloxy$, $C_{1-6}alkylthio$, aryl $C_{1-6}alkylthio$, arylcarbonyl, $HO(-CH_2-CH_2-O)_n$, $C_{1-6}alkyloxy(-CH_2-CH_2-O)_n$, aryl $C_{1-6}alkyloxy(-CH_2-CH_2-O)_n$, amino, mono-or di($C_{1-6}alkyl$)amino, $C_{1-6}alkyloxycarbonylamino$ and aryl;

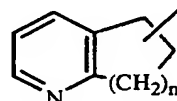
- 15 R^1 is a bicyclic heterocycle selected from quinolinyl, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, pyridopyridyl, naphthiridinyl, 1H-imidazo[4,5-b]pyridinyl, 3H-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]pyridinyl, 2,3-dihydro-1,4-dioxino[2,3-b]pyridyl or a radical of formula



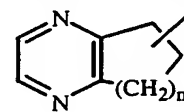
(c-1)



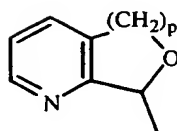
(c-2)



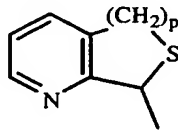
(c-3)



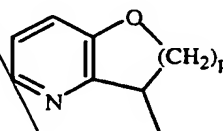
(c-4)



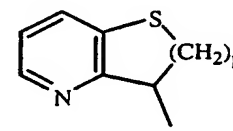
(c-5)



(c-6)



(c-7)



(c-8)

- 20 and said bicyclic heterocycles may optionally be substituted in either of the two cycles with 1 or where possible more, such as 2, 3 or 4, substituents selected from halo, hydroxy, amino, cyano, carboxy, $C_{1-6}alkyl$, $C_{1-6}alkyloxy$, $C_{1-6}alkylthio$, $C_{1-6}alkyloxy-C_{1-6}alkyl$, aryl, aryl $C_{1-6}alkyl$, aryl $C_{1-6}alkyloxy$, hydroxy $C_{1-6}alkyl$, mono-or di($C_{1-6}alkyl$)amino, mono-or di($C_{1-6}alkyl$)amino $C_{1-6}alkyl$, polyhalo $C_{1-6}alkyl$, $C_{1-6}alkylcarbonylamino$, $C_{1-6}alkyl-SO_2-NR^{5c}$, aryl- SO_2-NR^{5c} , $C_{1-6}alkyloxycarbonyl$, $-C(=O)-NR^{5c}R^{5d}$, $HO(-CH_2-CH_2-O)_n$, halo- $(-CH_2-CH_2-O)_n$, $C_{1-6}alkyloxy(-CH_2-CH_2-O)_n$, aryl $C_{1-6}alkyloxy(-CH_2-CH_2-O)_n$ and mono-or di($C_{1-6}alkyl$)amino- $(-CH_2-CH_2-O)_n$;
- 25 each n independently is 1, 2, 3 or 4;
each m independently is 1 or 2;

each p independently is 1 or 2;

each R² independently is hydrogen, formyl, C₁₋₆alkylcarbonyl, Hetcarbonyl, pyrrolidinyl, piperidinyl, homopiperidinyl, C₃₋₇cycloalkyl substituted with N(R⁶)₂, or C₁₋₁₀alkyl substituted with N(R⁶)₂ and optionally with a second, third or fourth

5 substituent selected from amino, hydroxy, C₃₋₇cycloalkyl, C₂₋₅alkanediyl, piperidinyl, mono-or di(C₁₋₆alkyl)amino, C₁₋₆alkyloxycarbonylamino, aryl and aryloxy;

R³ is hydrogen, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, arylC₁₋₆alkyl or arylC₁₋₆alkyloxy;

R⁴ is hydrogen, C₁₋₆alkyl or arylC₁₋₆alkyl;

R^{5a}, R^{5b}, R^{5c} and R^{5d} each independently are hydrogen or C₁₋₆alkyl; or

10 R^{5a} and R^{5b}, or R^{5c} and R^{5d} taken together form a bivalent radical of formula -(CH₂)_s- wherein s is 4 or 5;

R⁶ is hydrogen, C₁₋₆alkyl, formyl, hydroxyC₁₋₆alkyl, C₁₋₆alkylcarbonyl or C₁₋₆alkyloxycarbonyl;

15 aryl is phenyl or phenyl substituted with 1 or more, such as 2, 3 or 4, substituents selected from halo, hydroxy, C₁₋₆alkyl, hydroxyC₁₋₆alkyl, polyhaloC₁₋₆alkyl, and C₁₋₆alkyloxy;

Het is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl.

20 2. A compound according to claim 1 wherein -a¹=a²-a³=a⁴- is a radical of formula (a-1), (a-2) or (a-3).

3. A compound according to claim 1 or 2 wherein Q is a radical of formula (b-5) wherein v is 2 and Y¹ is -NR²-.

25 4. A compound according to anyone of claims 1 to 3 wherein R² is C₁₋₁₀alkyl substituted with NHR⁶.

30 5. A compound according to anyone of claims 1 to 4 wherein G is a direct bond or C₁₋₁₀alkanediyl optionally substituted with one, two or three substituents selected from hydroxy, C₁₋₆alkyloxy, arylC₁₋₆alkyloxy, HO(-CH₂-CH₂-O)_n-, C₁₋₆alkyloxy(-CH₂-CH₂-O)_n-, arylC₁₋₆alkyloxy(-CH₂-CH₂-O)_n-.

35 6. A compound according to claim 1 wherein the compound is selected from (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-4-methyl-1-[1-(8-quinolinyl)ethyl]-1H-benzimidazol-2-amine monohydrate; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-bromo-5,6,7,8-tetrahydro-8-quinolinyl)-1H-benzimidazol-2-amine trihydrochloride trihydrate; (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-4-methyl-1H-benzimidazol-

Sub
A1

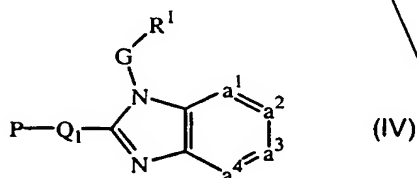
2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(1-methyl-1*H*-benzimidazol-4-yl)methyl]-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(ethoxy-8-quinolinylmethyl)-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-(5,6,7,8-tetrahydro-5-quinoxaliny)-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-7-methyl-3-(8-quinolinylmethyl)-3*H*-imidazo[4,5-*b*]pyridin-2-amine tetrahydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-7-methyl-3-(8-quinolinylmethyl)-3*H*-imidazo[4,5-*b*]pyridin-2-amine tetrahydrochloride monohydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(8-quinolinylmethyl)-1*H*-imidazo[4,5-*c*]pyridin-2-amine trihydrochloride dihydrate; *N*-[1-(2-aminoethyl)-4-piperidinyl]-4-methyl-1-(8-quinolinylmethyl)-1*H*-benzimidazol-2-amine; *N*-[1-(8-quinolinylmethyl)-1*H*-benzimidazol-2-yl]-1,3-propanediamine trihydrochloride monohydrate; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1*H*-benzimidazol-2-amine trihydrochloride dihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(8-quinolinylmethyl)-1*H*-imidazo[4,5-*b*]pyridine-2-amine trihydrochloride dihydrate; (\pm)-*N*-[1-[1-(aminomethyl)-2-methylpropyl]-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-3-(2-quinolinylmethyl)-3*H*-imidazo[4,5-*b*]pyridin-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(1-isoquinolinylmethyl)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; *N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(5,6,7,8-tetrahydro-5-quinoxaliny)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-3-(quinolinylmethyl)-3*H*-imidazo[4,5-*b*]pyridin-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-(8-quinolinylmethyl)-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-4-methyl-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(5,6,7,8-tetrahydro-2,3-dimethyl-5-quinoxaliny)-1*H*-benzimidazol-2-amine trihydrochloride trihydrate; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1*H*-benzimidazol-2-amine; (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(3-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-1*H*-benzimidazol-2-amine trihydrochloride monohydrate; (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(3-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-4-methyl-1*H*-benzimidazol-2-amine trihydrochloride dihydrate; (\pm)-*N*-[1-(2-

Sub
Al

100393-1003

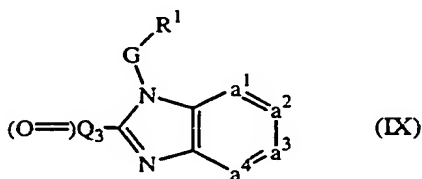
aminoethyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-4-methyl-1*H*-benzimidazol-2-amine monohydrate; (±)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-3-(8-quinolinylmethyl)-3*H*-imidazo[4,5-*c*]pyridin-2-amine trihydrochloride tetrahydrate; (±)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-3-(8-quinolinylmethyl)-3*H*-imidazo[4,5-*b*]pyridin-2-amine; (±)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-[(1-methyl-1*H*-benzimidazol-4-yl)methyl]-1*H*-benzimidazol-2-amine; (±)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxaliny)-4-methyl-1*H*-benzimidazol-2-amine; a prodrug, *N*-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof.

7. A compound according to any one of claims 1 to 6 for use as a medicine.
8. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as described in any one of claims 1 to 6.
9. A process of preparing a composition as claimed in claim 8, characterized in that, a pharmaceutically acceptable carrier is intimately mixed with a therapeutically effective amount of a compound as described in any one of claims 1 to 6.
10. An intermediate of formula



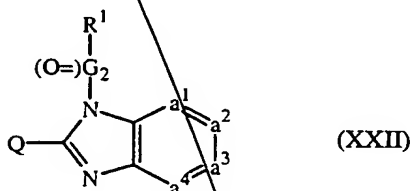
with R^1 , G and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, P being a protective group, and Q_1 being defined as Q according to claim 1 but being devoided of the R^2 or R^6 substituent.

11. An intermediate of formula



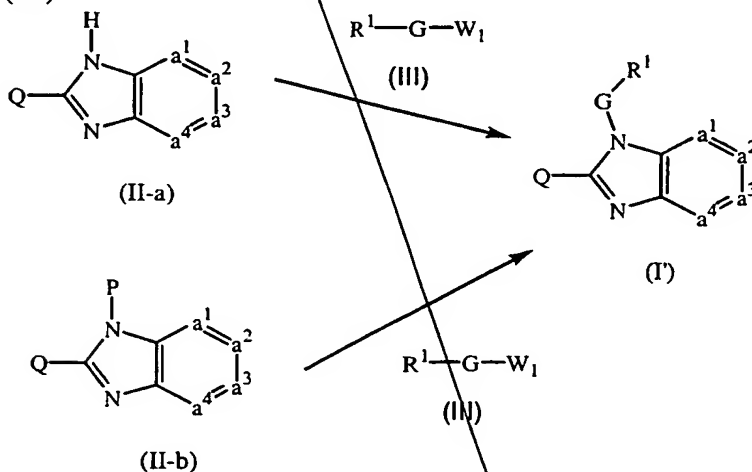
with R^1 , G and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $(O=)Q_3$ being a carbonyl derivative of Q, said Q being defined according to claim 1, provided that it is devoided of the NR^2R^4 or NR^2 substituent.

- 5 12. An intermediate of formula



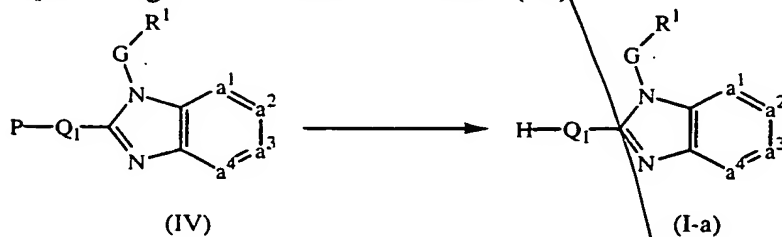
with R^1 , Q and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $(O=)G_2$ being a carbonyl derivative of G, said G being defined according to claim 1.

- 10 13. A process of preparing a compound as claimed in claim 1, characterized by,
a) reacting an intermediate of formula (II-a) or (II-b) with an intermediate of formula (III)



- 15 with R^1 , G, Q and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and W_1 being a suitable leaving group, in the presence of a suitable base and in a suitable reaction-inert solvent;

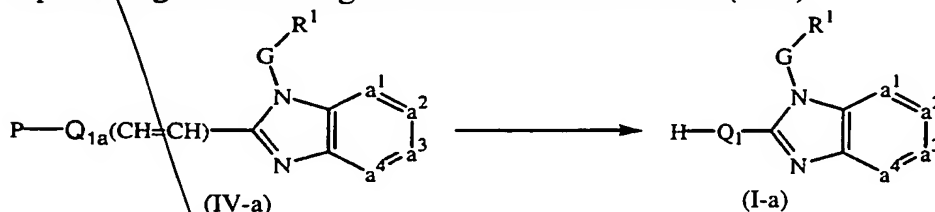
- b) deprotecting an intermediate of formula (IV)



-90-

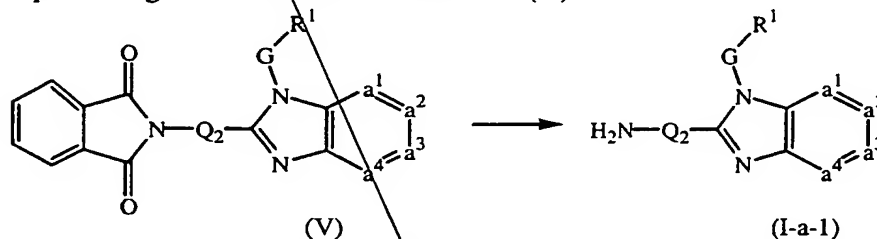
with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, $H-Q_1$ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen, and P being a protective group;

- 5 c) deprotecting and reducing an intermediate of formula (IV-a)



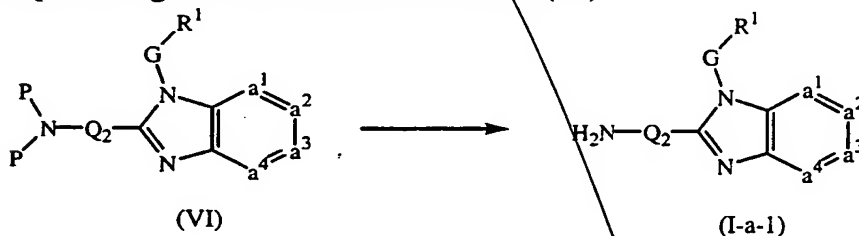
with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, $H-Q_1$ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen, $Q_{1a}(CH=CH)$ being defined as Q_1 provided that Q_1 comprises an unsaturated bond, and P being a protective group;

- 10 d) deprotecting an intermediate of formula (V)



with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H_2N-Q_2 being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen;

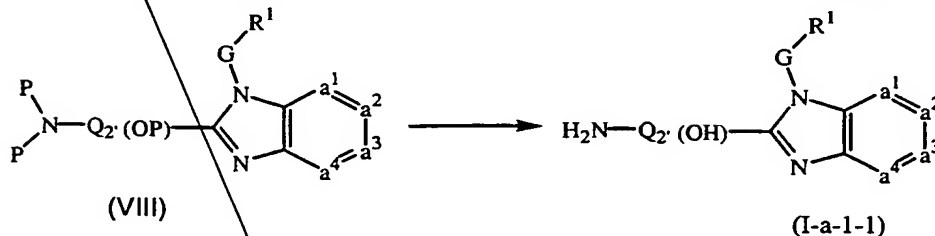
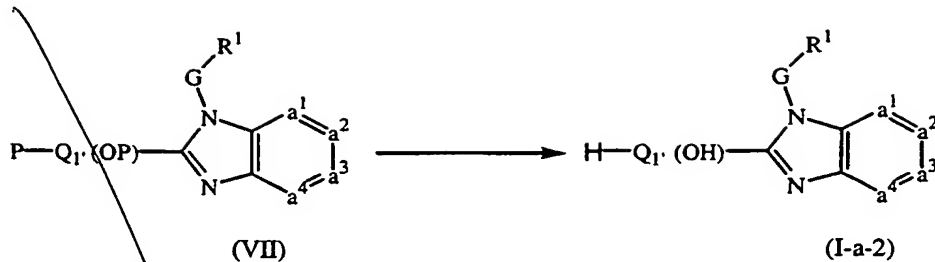
- 15 e) deprotecting an intermediate of formula (VI)



20 with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H_2N-Q_2 being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen, and P being a protective group;

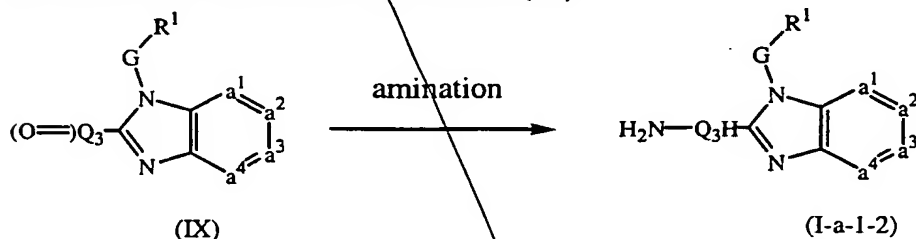
- f) deprotecting an intermediate of formula (VII) or (VIII)

-91-



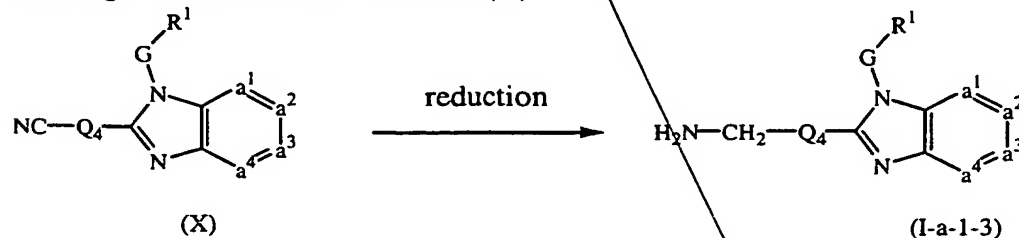
with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, $H-Q_1(OH)$ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen and provided that Q comprises a hydroxy moiety, $H_2N-Q_2(OH)$ being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen and provided that Q comprises a hydroxy moiety, and P being a protective group;

g) amination of an intermediate of formula (IX)



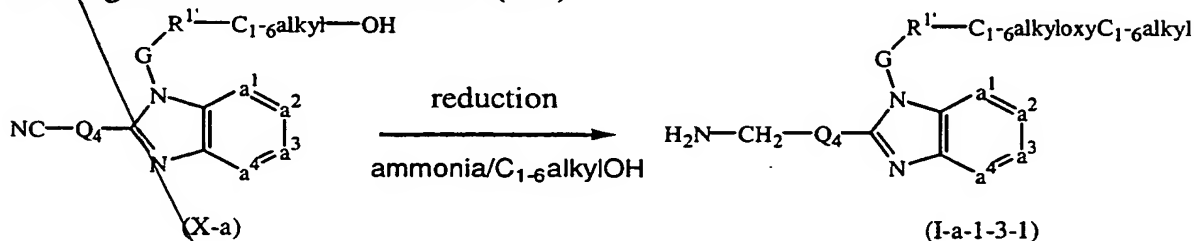
with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H_2N-Q_3H being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen, and the carbon adjacent to the nitrogen carrying the R^6 , or R^2 and R^4 substituents contains at least one hydrogen, in the presence of a suitable amination reagent;

h) reducing an intermediate of formula (X)



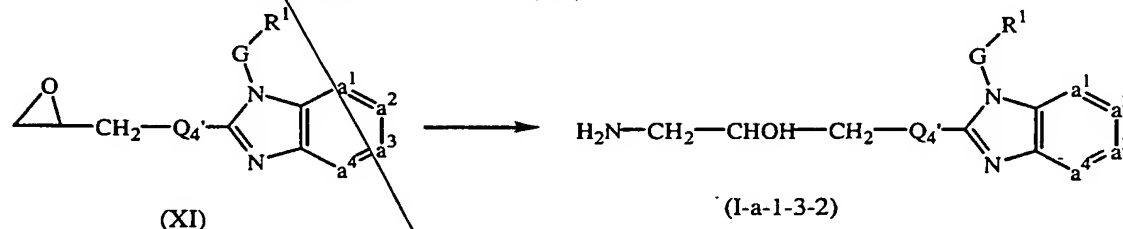
with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $H_2N-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $-CH_2-NH_2$ moiety, in the presence of a suitable reducing agent;

- i) reducing an intermediate of formula (X-a)



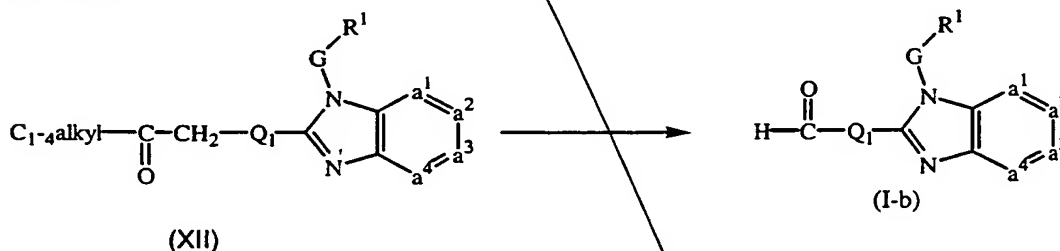
with G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, $H_2N-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $-CH_2-NH_2$ moiety, and $R^{1'}$ being defined as R^1 according to claim 1 provided that it comprises at least one substituent, in the presence of a suitable reducing agent and suitable solvent;

- j) amination of an intermediate of formula (XI)



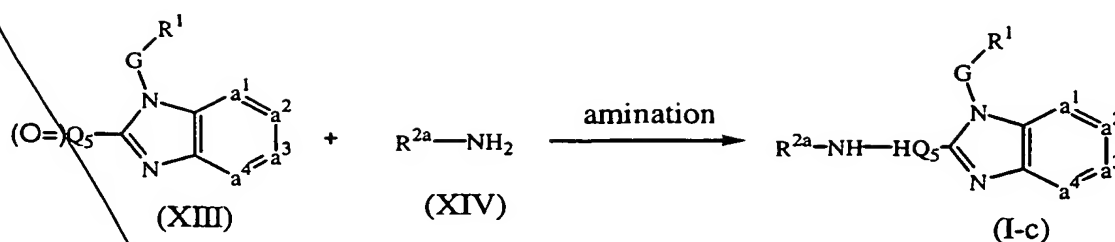
with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $H_2N-CH_2-CHOH-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $CH_2-CHOH-CH_2-NH_2$ moiety, in the presence of a suitable amination reagent;

- k) reacting an intermediate of formula (XII) with formic acid, formamide and ammonia



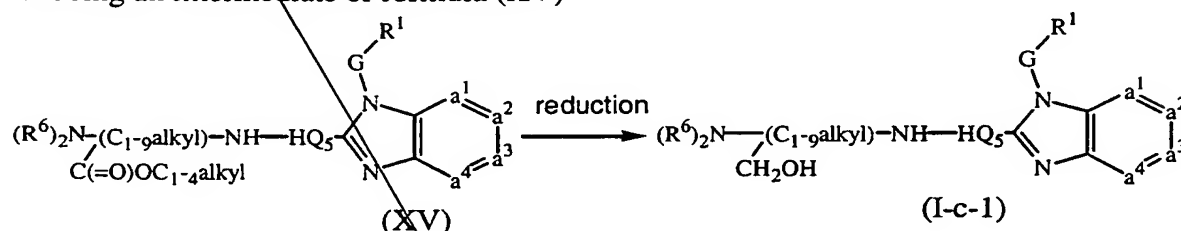
with R^1 , G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and $H-C(=O)-Q_1$ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is formyl;

- l) amination of an intermediate of formula (XIII) by reaction with an intermediate of formula (XIV)



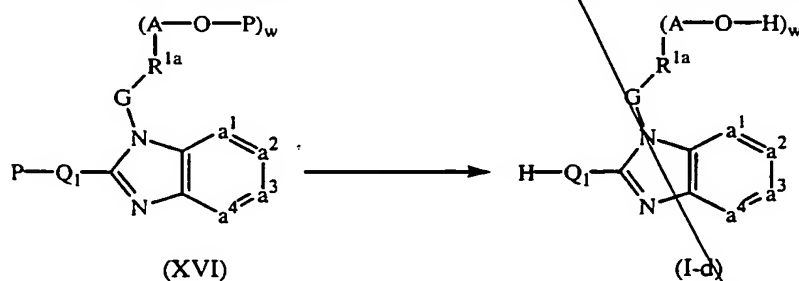
with R¹, G, and -a¹=a²-a³=a⁴- defined as in claim 1, and R^{2a}-NH-HQ₅ being defined as Q according to claim 1 provided that R² is other than hydrogen and is represented by R^{2a}, R⁴ is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R² and R⁴ substituents, carries also at least one hydrogen atom, in the presence of a suitable reducing agent;

m) reducing an intermediate of formula (XV)

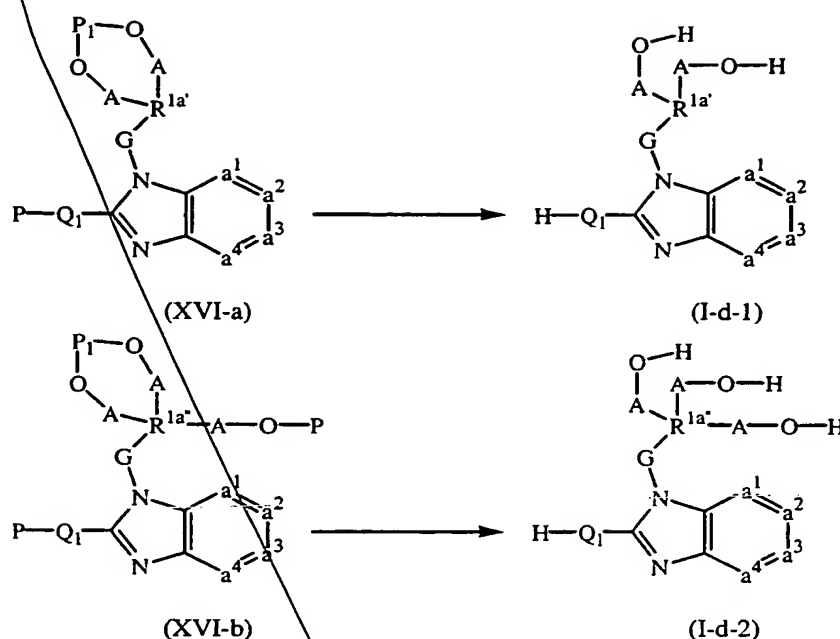


with R¹, G, and -a¹=a²-a³=a⁴- defined as in claim 1, and (R⁶)₂N-[(C₁₋₉alkyl)CH₂OH]-NH-HQ₅ being defined as Q according to claim 1 provided that R² is other than hydrogen and is represented by C₁₋₁₀alkyl substituted with N(R₆)₂ and with hydroxy, and the carbon atom carrying the hydroxy, carries also two hydrogen atoms, and provided that R⁴ is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R² and R⁴ substituents, carries also at least one hydrogen atom, with a suitable reducing agent;

n) deprotecting an intermediate of formula (XVI), (XVI-a) or (XVI-b)

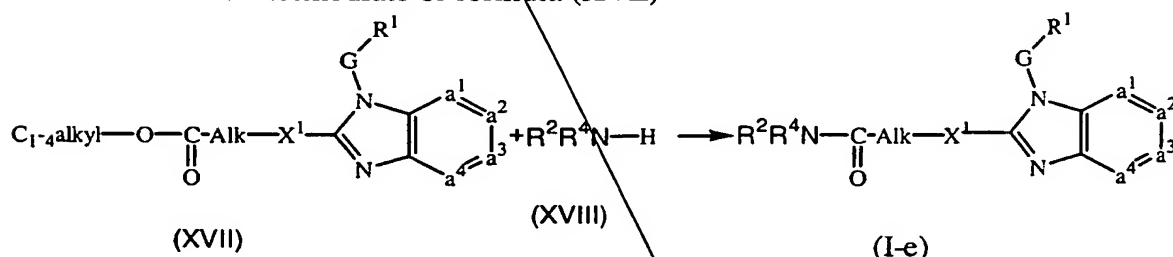


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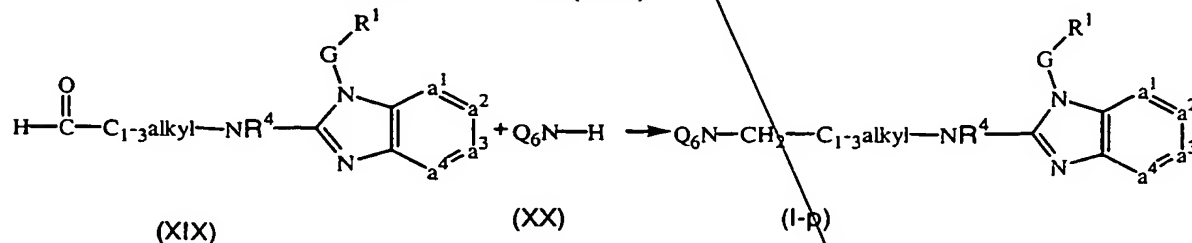
with G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and H-Q₁ being defined as Q according to claim 1 provided that R² or at least one R⁶ substituent is hydrogen, and R^{1a}-(A-O-H)_w, R^{1a'}-(A-O-H)₂ and R^{1a''}-(A-O-H)₃ being defined as R¹ according to claim 1 provided that R¹ is substituted with hydroxy, hydroxyC₁₋₆alkyl, or HO(-CH₂-CH₂-O)_n-, with w being an integer from 1 to 4 and P or P₁ being a suitable protecting group, with a suitable acid.

o) amination of an intermediate of formula (XVII)



with R¹, G, $-a^1=a^2-a^3=a^4-$, Alk, X¹, R² and R⁴ defined as in claim 1, in the presence of a suitable amination agent;

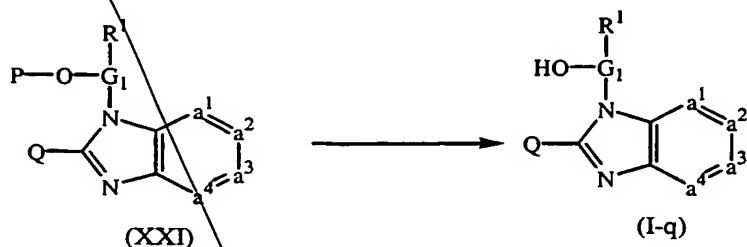
p) amination of an intermediate of formula (XIX)



with R¹, G, and $-a^1=a^2-a^3=a^4-$ defined as in claim 1, and Q₆N-CH₂-C₁₋₃alkyl-NR⁴

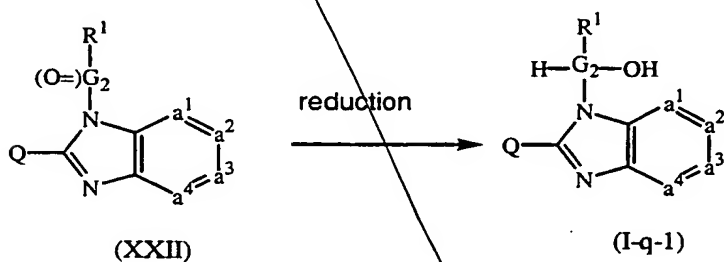
being defined as Q according to claim 1 provided that in the definition of Q, X² is C₂₋₄alkyl-NR⁴, in the presence of a suitable amination agent;

- q) deprotecting an intermediate of formula (XXI)



with R¹, Q, and -a¹=a²-a³=a⁴- defined as in claim 1, and HO-G₁ being defined as G according to claim 1 provided that G is substituted with hydroxy or HO-(CH₂CH₂O-)_n;

- r) reducing an intermediate of formula (XXII)



with R¹, Q, and -a¹=a²-a³=a⁴- defined as in claim 1, and H-G₂-OH being defined as G according to claim 1 provided that G is substituted with hydroxy and the carbon atom carrying the hydroxy substituent carries also at least one hydrogen, in the presence of a suitable reducing agent.

and, if desired, converting compounds of formula (I) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali, or converting the base addition salt into the free acid by treatment with acid; and, if desired, preparing stereochemically isomeric forms, metal complexes, quaternary amines or N-oxide forms thereof.

14. A product containing (a) a compound as defined in claim 1, and (b) another antiviral compound, as a combined preparation for simultaneous, separate or sequential use in the treatment or the prevention of viral infections.

Sub
A1

15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredients (a) a compound as defined in claim 1, and (b) another antiviral compound.
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A2

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